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On the phenomenology of enzyme-substrate recognition

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Abstract : A model for enzyme-substrate recognition is presented in which both the substrate and the enzyme are represented by Hilbert space operators A and W of trace class; and the recognition proceeds by the evaluation of the trace functional $Tr(AW)$. The eigen values of A (and analogously of W) are interpreted as response values that the substrate can give to an enzyme. The non-commutativity or otherwise of A and W permits to incorporate both the induced-fit hypothesis as well as the lock-and-key ansatz in the model. Key features of recognition like finite power of resolution, the specificity of the recognition states as well as the duality during recognition between the enzyme and the substrate are derived. Several refined aspects of recognition like invariance under change of state in induced-fit situation, a quantitative measure of recognition as well as the existence of a complete set of simultaneous recognition states in the lock-and-key situation are deduced. The present model substantially refines earlier models proposed by Edelstein and Rosen and by Louie, Richardson and Swaminathan.

Keywords : Enzyme-substrate recognition, Hilbert space operator, eigen values and eigen space, induced-fit theory, lock and key hypothesis.

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1. Introduction

The present paper is aimed at contributing to a phenomenological description of the enzyme-substrate recognition. A model for enzyme-substrate recognition has been proposed by Edelstein and Rosen [1] (ER model) in which given a bounded subset K of the physical space E^3 enclosing the enzyme-substrate system, a state of the substrate is represented by a continuous real valued function f on K, and enzyme state is represented by a real valued function α of bounded variation defined on K, and the enzyme-substrate recognition is achieved by the evaluation of the Steltjes integral $\int_K f d\alpha$. This model admits very many satisfactory biological consequences [1].

In view of the boundedness of K, the space $C(K)$ of all continuous functions on K is contained in the space $L^2(K)$ of all square integrable Lebesgue measurable functions on K. This led Louie, Richardson and Swaminathan [2] (LRS model) to extend the ER-model in which both the substrate state and the enzyme state are represented by functions f and g in $L^2(K)$; and the recognition is achieved by the evaluation of the L^2-inner product $\langle f,g\rangle = \int_K f(s)\,\overline{g(s)}\,dm(s)$. Besides retaining the advantages of ER-model and bringing in the mathematically rich all pervading Hilbert space L^2(K) into the scheme, the LRS-model admits three features : it incorporates the response-tensor (represented mathematically by a dyadic) which is an important component in the phenomenological calulus for complex systems developed by Richardson, Louie and Swaminathan [3]; it includes the enzyme-substrate complex and the modified enzyme-product complex of the catalytic reaction; and it places the

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substrate state and the enzyme state mathematically on equal footings. It may be noted that both the ER-model and the LRS-model look to recognition as a process of measurement in which either of the substrate and the enzyme is an observable performing a measurement on the other.

Biologically significant features of the enzyme-substrate recognition are the high degree of specificity, the requirement of appropriate three dimensional configurations of the molecules for the biological activity, as well as the finite power of resolution. Despite specificity, the recognizing molecule fails to distinguish between two sufficiently close states of the other molecule – a key feature in drug design. There are two ansatz put forward to explain recognition [4].

(*i*) *Lock-and-key model :*

The enzyme and the substrate possess rigid structures, the active site of the enzyme being structurally complementary to the substrate, so that it fits with the substrate.

(*ii*) *Induced-fit-theory :*

The substrate causes changes in the geometry of the enzyme while fitting into active site; and in the process, induces proper orientation of catalytic groups.

The ER-model and LRS-model do not incorporate above ansatzs (i) and (ii).

Now in the light of the fact that the above models view enzyme-substrate recognition as a process of measurement, above ansatz (ii) has a close analogue in Quantum Mechanics wherein measurement of an observable on the system interacts with the system resulting in a change of state [5]. This motivates us to develop the present model in which the formalism of Quantum Theory is adapted to describe the enzyme-substrate recognition, though we do not use any physical principles of Quantum Mechanics. The followings are the salient features of the present model.

(i) With every enzyme-substrate system, a Hilbert space H is associated such that the recognition states of the enzyme and the substrate are represented by positive trace-class operators A and W, respectively on H. This unfolds the role of H that appears in LRS-model.

(ii) The recognition of a substrate by an enzyme (and *vice-versa*) is achieved by the evaluation of the trace functional $Tr(AW)$ which gives a quantitative measure of recognition.

(iii) Every enzyme state A (and analogously every substrate state W) admits a discrete set (a_n) of intrinsic response values that it can give to any enzyme. At the present phenomenological level, this intrinsic recognition property is like the mass or charge of a particle, whose origin and explanation are beyond phenomenology. These response values are precisely the eigen values of A, the eigen space Λ_{a_n} of an eigen value a_n being the enzyme state in which the enzyme admits precise response value a_n.

(iv) In an enzyme state A which is not an eigen state, the response value of the enzyme is only probabilistically defined, and $Tr(AW)$ = probabilistic average of the product of response values of the enzyme and the substrate states.

(v) During recognition, a change of enzyme state $A \rightarrow A^1$ and a change of the substrate state $W \rightarrow W^1$ occur. This incorporates the induced-fit hypothesis. In fact, this happens precisely when $AW \neq WA$. On the other hand, $W = W^1$, $A = A^1$ if and only if $AW = WA$ exhibiting the lock-and-key phenomenon in this case. Thus, the commutativity of operations A and W manifests the structural complementarity of the enzyme and the substrate.

We demonstrate that the present model not only incorporates both the ER-model and the LRS-model, but also refines them. In the present model, the enzyme-substrate complex is represented by $A \otimes W$, whereas the modified enzyme-product complex is given by $(Tr(A^2))^{-1}A \otimes (Tr(A^2))W$. In fact, the whole formalism can be schematically represented by using the Hilbert space $C^2(H)$ of all Hilbert-Schmidt operators on H, thereby refining the scheme proposed by Swaminathan [6]. We exhibit the finite power of resolution, the specificity of the recognizing states as well as the perfect duality between the enzyme and the substrate during recognition. Several refined aspects of recognition like the invariance under change of states in induced-fit situations as well as the existence of complete set of simultaneous recognition states in lock-and-key situation are derived.

2. Hilbert spaces

Postulate 1 : Given an enzyme-substrate system, there exists a Hilbert space H associated with the system.

The Hilbert space H associated with a given enzyme-substrate system provides the basic mathematical background in the framework of which the system is to be described. In the simplest case of a system consisting of a single enzyme recognizing a single substrate molecule enclosed in a bounded subset K of the physical space E^3, we can take H to be the space $L^2(K,m)$ with the inner product $\langle f,g\rangle = \int_K f(s)\,\overline{g(s)}\,dm(s)$, m denoting the Lebesgue measure on K. This is the formalaism suggested in [2,6] extending the formalism of [1] wherein the underlying mathematical space is $C(K)$ which is contained in $L^2(K)$. To include the possibility of allowing other Hilbert spaces possibly in a more complex system (*e.g.* multi-enzyme systems) and in view of the simplicity of the notations, we work in the abstract Hilbert space H.

3. Recognition states of the substrate

By a *state* of the system, we mean a parameter or mathematical entity containing all instantaneous information about the system explicitly or implicitly. A given system can admit different states. Given a substrate molecule, there are different quantum mechanical states of the molecule; and also there are different topological states of the molecule depending on its configuration, shape, geometry, orientation *etc.* By a *recognition state* of the molecule, we mean a state containing all information relevant to enzyme-substrate recognition.

Postulate II(a) :

A recognition state of the substrate is represented by a positive trace class operator W on H.

Any positive trace class operator is of the form [7]

$$W = \sum_{n=1}^{\infty} w_n \tag{3.1}$$

where $w_n \geq 0$ are the eigen values of W, Λ_{w_n} is the orthogonal projection on the eigen space of the eigen value w_n and $\sum w_n < \infty$. Counting w_n's according to their multiplicities, W is also of the form

$$W = \sum_{n=1}^{\infty} w_n e_n \otimes e_n\,, \tag{3.2}$$

where (e_n) is an orthonormal system. The trace is given by $Tr(W) = \sum w_n$ counting according to multiplicities, that is, $Tr(W) = \sum k_n w_n$, k_n being the multiplicity of w_n.

The biological interpretations of the eigen values and the eigen spaces are given by the following postulate which presumes that at the phenomenological level every recognition state has a recognition power. No physical meaning is attached to this recognition power at this stage, though we believe that it can be a statistical manifestation of quantum mechanical attributes underlying recognition. Of course, its origin is beyond phenomenology.

Postulate II(b) :

(i) Any recognition state W of the substrate admits a discrete countable set of intrinsic response values giving the possible values of (measures of) responses that W gives to an enzyme state during recognition.

(ii) These response values are given by the eigen values (w_n) of W.

(iii) The eigen state Λ_{w_n} is the state of the substrate in which the response value is precisely w_n.

If $f \perp g$ are both in $\Lambda_{w_n}(H)$ then $Wf = w_n f$, $Wg = w_n g$ showing that $f \otimes f$ and $g \otimes g$ are two distinct states in which the enzyme admits the same response values.

The response values (w_n) represent the intrinsic property of the substrate state W independent of the enzyme which recognizes W. They give the possible values of the recognition power of the substrate W in different states. As in ER-model, we adopt the point of view that either of the substrate and the enzyme recognizes the other, *i.e.* recognition is an interactive process in which both the enzyme and substrate are involved. The discreteness of (w_n) amounts to the finite power of resolution to be clarified later. The above postulate is further refined as follows.

Postulate II(c) :

(i) The eigen states Λ_{w_n} are the only substrate states that admit precise response values.

(ii) In the state W, the response value is only probabilistically defined; and $\dfrac{Tr(W\Lambda_{w_n})}{Tr(W)}$ = the probability that the state W admits response value w_n.

It may be noted that $W\Lambda_{w_n} = w_n\Lambda_{w_n}$ and $Tr(W\Lambda_{w_n}) = k_n w_n$, k_n being the multiplicity of the eigen value w_n. The above probabilistic interpretation demands that

$\sum_1^\infty \Lambda_{w_n} Tr(W\Lambda_{w_n}) = Tr(W)$. This would be satisfied provided that $\sum_1^\infty \Lambda_{w_n} = 1$, *i.e.*, the ranges of the projection operators Λ_{w_n} span the whole space H. This leads us to introduce the following completensess postulate the role of which will be discussed later.

Postulate II(d) :

The space H is the closed linear span of the eigen spaces H_{w_n}, $n = 1, 2, 3,$..... *In other word, in the expression (3.2),* (e_n) *forms an orthonormal basis.*

Let $C^1(H)$ be the Banach space of all trace class operators $W = \sum w_n \Lambda w_n$ with the response norm (trace norm) $\|W\|_1 = \sum |w_n|$ interpreted as a measure of the intrinsic recognition power of W. Let $C^2(H)$ be the space of all Hilbert-Schmidt operators on H with norm $\|T\|_2 = Tr(T^*T)^{1/2}$. In fact, $C^2(H)$ is a Hilbert space with inner product $\langle T,S\rangle = Tr(S^*T)$ and $\|T\|_1 \geq \|T\|_2 \geq \|T\|$: = operator norm of T and $C^1(H) \subset C^2(H)$.

4. Recognition states of an enzyme

Let W be a recognition state of a substrate. Then any positive operator A on H, not necessary bounded, such that $Tr(AW) < \infty$ can be taken to represent an enzyme state; and for all $A \in B(H)$, we have that $Tr(AW) < \infty$. However, we need to incorporate the following in our formalism.

(i) Both the enzyme recognition state and the substrate recognition state should be on an equal footing so that during recognition, each recognizes the other.

(ii) The total recognition power of the enzyme should be finite.

In order to achieve this, we introduce the following analogue of Postulate (II) of the previous section.

Postulate III :

(a) A recognition state of an enzyme is represented by a positive trace class operator A on H.

(b) (i) Any recognition state A of the enzyme admits a countable discrete set of intrinsic response values giving the possible values of measure of responses that the enzyme gives to any substrate.

(ii) These values are given by the eigen values (a_n) *of A.*

(iii) The eigen state Λ_{a_n} *represents that recognition state of the enzyme in which the intrinsic response value is precisely* a_n.

(c) (i) The eigen states Λ_{a_n} *are the only recognition states that admit precise response values.*

(ii) In the state A, the response value is only probabilistically defined and $\frac{Tr(A\Lambda_{a_n})}{Tr(A)}$ = *probability that the state A admits response value* a_n.

(d) The space H is the closed linear span of the eigen spaces H_{a_n}, $n = 1, 2, 3,$.....

Potulate IV : The measure of the recognition of the substrate state W by an enzyme state A is given by Tr(AW).

Thus, $Tr(AW)$ can be interpreted as the measure of response that the substrate gives to the enzyme during recognition. Now, the operator theoretic theorem *i.e.* $Tr(AW) = Tr(WA)$ manifests the desirable biological fact that during recognition, the response that substrate state W gives to an enzyme state A equals the response that the enzyme state A gives to the substrate W. This exhibits the duality inherent in the recognition process discussed in details in [1]; and this happens in spite of the fact that $AW \neq WA$ in general.

The operator theoretic inequality

$$|Tr(A_1W_1) - Tr(A_2W_2)| \leq \|W_1\| \, \|A_1 - A_2\|_1 + \|A_2\| \, \|W_1 - W_2\|_1$$

implies that the recognition process is jointly continuous with respect to the response norms of both the enzyme and the substrate. This exhibits the sensitivity of recognition with respect to response norms. This also shows that substrate states having sufficiently near response norms are recognized sufficiently identically by an enzyme. This sensitivity of the recognition process with respect to the response norms compares with the following indistinguishability result. We say that two substrate states W_1 and W_2 are *indistinguishable* by an enzyme state A if $Tr(AW_1) = Tr(AW_2)$.

Theorem 1

Distinct states of the substrate belonging to the same eigen space of the enzyme and having the same norms are not distinguished by the enzyme. Dually distinct state

of the enzyme belonging to the same eigen space of the substrate and having the same norms are not distinguished by the substrate.

Proof : Let a_n be a fixed eigen value of A, the corresponding eigen space being $H_{a_n} = \Lambda_{a_n}(H)$. Let f and g be in H_{a_n}, $\|f\| = \|g\|$. The substrate states determined by f and g are given by the 1-dimensional operators $f \otimes f$ and $g \otimes g$. Let A be an enzyme state. Then an easy computation gives $TrA(f \otimes f) = a_n\|f\|^2$; and $TrA(g \otimes g) = a_n\|g\|^2$. Thus $Tr(A(f \otimes f)) = Tr(A(g \otimes g))$.

The conclusion of the following theorem quantitatively manifests the duality between the enzyme and the substrate inherent in the process of recognition, which is qualitatively discussed in [1].

Theorem 2

Let $Tr(W) = Tr(A) = 1$. In a recognition process in which a substrate state W is recognized by an enzyme state A, one has the measure of recognition

= *statistical average of the products of response values of A and W*

= *statistical average response that W gives to A*

= *statistical average response that A gives to W.*

Proof : In usual notations, let $A = \sum_1^\infty a_n \Lambda_{a_n}$, $W = \sum_{k=1}^\infty w_k \Lambda_{w_k}$.

Then

$$Tr(AW) = \sum w_k Tr(A\Lambda_{w_k})$$

= $\sum$ ($w_k \times$ probability that W gives response w_k to A)

= average response of W to A;

$$\text{and } Tr(AW) = Tr(WA) = \sum a_n Tr(W\Lambda_{a_n})$$

= $\sum$ ($a_n \times$ probability that A gives response a_n to W)

= average response of A to W;

Further,

$$Tr(AW) = Tr\left(\sum a_n \Lambda_{a_n}\right)\left(\sum w_k \Lambda_{w_k}\right)$$

$$= \sum_{n,k=}^{\infty} a_n w_k Tr(\Lambda_{a_n} \Lambda_{w_k})$$

$$= \sum_{n,k=1}^{\infty} a_n w_k$$ (joint probability that A has response a_n and W gives response w_k).

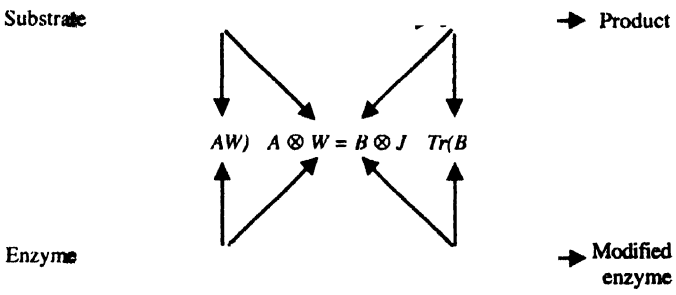

Figure 1. A schematic representation of enzyme substrate recognition.

Here, $\boldsymbol{H}$ is the conjugate space of H, and tensor products are completed tensor products. A, W, J and B are in $C^2(H) \simeq H \otimes \boldsymbol{H}$, $A \otimes W = B \otimes J$ in $C^2(H) \otimes C^2(\boldsymbol{H}) \simeq C^2(H \otimes \boldsymbol{H})$. Also $A \otimes W$ represents enzyme substrate complex,

$J = Tr(A^2)W$ represents the product,

$B = (Tr(A^2))^{-1} A$ represents the modified enzyme.

$B \otimes J$ = modified enzyme-product complex.

This scheme is analogous to the one in Ref. [6] in the sense that Hilbert space H is replaced by the Hilbert space $C^2(H)$ to accommodate the more refined formulation of the present model; and the somewhat out-dated dyadics are replaced by the tensor products of operators. In fact the dyadic space $T_1^1(H)$ [6] is contained in $C^2(H)$. The states $f \otimes f$ defined by f in H are the analogues of the pure states in Quantum Theory.

We consider the following two particular cases.

(a) Integral operators :

Let $H = L^2(K,m)$. Then $C^2(H) \simeq L^2(K \times K, m \times m)$. An integral operator on $L^2(K,m)$ is an operator of the form

$$(I_k f)(x) = \int_k K(x,y) f(y) dm(y)$$

for an appropriate function k called the *kernel* of the operator I_k. It is well known that I_k is a Hilbert-Schmedt

operator if and only $k \in L^2(K \times K, m \times m)$. Now let $A = I_a$ and $W = I_w$ be the integral operators representing enzyme and the substrate respectively. Then the operators $AW = I_p$ and $WA = I_q$ are integral operators having kernels

$$p(x, y) = \int_K a(n, z)w(z, y)dm(z)$$

and

$$q(x, y) = \int_K w(x, z)a(z, y)dm(z).$$

The measure of recognition is given by

$$Tr(AW) = \iint_{K\times K}\left[\int_K a(x, z)w(z, y)dm(z)\right]d^2m(x, y).$$

(b) Edelstein-Rosen model :

To derive the ER-model in the present formalism, let $f \in C(K)$ be a substrate state, $\alpha \in BV(K)$ be an enzyme state. Then α is differentiable almost everywhere on K and denoting the derivative of α by α'

$$\int_K fd\alpha = \int_K f\alpha' dm = < f, \alpha' >.$$

This is the ER-formalism. To fit it in the present formalism, we identify f with $\Lambda_f = f \otimes f$ 1-dimensional projection operator having range $\{\lambda f | \lambda \in C\}$ and α with $\Lambda_{\alpha'} = \alpha' \otimes \alpha'$. Notice that $\alpha' \in L^1(K,m)$, hence $\alpha' \in L^2(K,m)$. Then the measure of recognition of $f \otimes f$ by $\alpha' \otimes \alpha'$ is

$$Tr(\Lambda_f \Lambda_{\alpha'}) = \sum_n < (f \otimes f)(\alpha' \otimes \alpha')e_n, e_n >$$

$$= \sum_n < e_n, \alpha' >< \alpha', f >< f, e_n >$$

$$= < \alpha', f > \sum_n < f, e_n >< e_n, \alpha' >$$

$$= < \alpha', f >< f, \alpha' >$$

$$= |< \alpha', f >|^2 = \left|\int_K fd\alpha\right|^2 .$$

= measure of recognition of f by α.

This shows that the Edelstein-Rosen model is contained in the present model. In both ER-model and the LRS-models, a recognition state is of form f (f in H), whereas in the present model, a recognition state is assumed to be of form

$$W = \sum w_n f_n \otimes f_n .$$

Identifying f with $f \otimes f$, it follows that the present model accommodates more complex recognition states.

5. Recognition and change of states

Postulate V : Let W be a recognition state of a substrate having eigen values (w_n). Let A be a recognition state of the enzyme having eigen values (a_n). During the recognition of W by A (and simultaneously of A by W), there occurs a change of states $W \to W'$, $A \to A'$ where

$$W' = \sum_{n=1}^{\infty} \Lambda_{a_n} W \Lambda_{a_n} ,$$

$$A^1 = \sum_{n=1}^{\infty} \Lambda_{w_n} A \Lambda_{w_n}$$

The above postulate views recognition as a change of recognition states. We say that recognition states A and W are *complementary* if $AW = WA$. The following theorem is a biological interpretation of the statement that $AW = WA$ if and only if $W = A^1$ if and only if $A = A^1$. It shows that the present model permits both the lock-and-key phenomenon as well as the induced-fit phenomenon depending on the nature of the states involved, but never both simultaneously as is desirable.

Theorem 3

(a) There is no change of states during recognition if and only if the enzyme state and the substrate state are complementary to each other (lock-and-key ansatz)

(b) There occurs a change of state during recognition if and only if the enzyme state and the substrate state are not complementary (Induced-fit ansatz)

(c) During recognition, there is a change of enzyme state if and only if there is a change of substrate state.

The following refines Theorem 2 for complementary states.

Theorem 4

Let A and W be recognition states of an enzyme and a substrates complementary to each other and having

response values (a_n) and (w_k) respectively. Then there exists $\{g_{n_k}, k = 1, 2, \ldots\}$ in H such that the following hold.

(i) (g_{n_k}) is an orthonormal basis for H,

(ii) For each $k, g_{n_k} \otimes g_{n_k}$ is a state in which the enzyme admits precise response value a_{n_k} and the substrate admits precise response value w_{n_k} simultaneously.

(iii)

$$Tr(AW) = \sum_{k=1}^{\infty} a_{n_k} w_{n_k} .$$

This theorem is a reformulation of the joint eigen value theorem for commuting self-adjoint operators. It shows that in complementary states, the enzyme and the substrate admit joint response values and the corresponding joint response states form a complete set.

The next three results unfold several aspects of the phenomenology of the induced-fit phenomenon. The following theorem shows that quantitatively the recognition is invariant under the change of state in induced-fit phenomenon.

Theorem 5

Let $A \to A^1$, $W \to W^1$ be the change of states of the enzyme and the substrate molecule during the induced-fit phenomenon in recognition. Then, measure of recognition of W by A = measure of recognition of W^1 by A^1 = measure of recognition of W by A^1 = measure of recognition of W^1 by A.

Proof : Given

$$W = \sum_{1}^{\infty} w_n \Lambda_{w_n}, \quad A = \sum_{1}^{\infty} a_n \Lambda_{a_n} ,$$

we have by postulate *V*,

$$W^1 = \sum_{1}^{\infty} \Lambda_{a_n} W \Lambda_{w_n}, \quad A^1 = \sum_{1}^{\infty} \Lambda_{w_n} A \Lambda_{w_n} .$$

Then,

$$Tr(W^1) = Tr\left(\sum_{1}^{\infty} \Lambda_{a_n} W \Lambda_{a_n} \right)$$

$$= \sum_{1}^{\infty} Tr\left(W \Lambda_{a_n}^2\right)$$

$$= \sum_{1}^{\infty} Tr\left(W \Lambda_{a_n}\right)$$

$$= \sum_{k=1}^{\infty} \sum_{n=1}^{\infty} \langle W \Lambda_{a_n} e_k, e_k \rangle$$

$$= \sum_{k=1}^{\infty} \left\langle W \left| \sum_{n=1}^{\infty} \Lambda_{a_n} e_k \right|, e_k \right\rangle$$

$$= \sum_{k=1}^{\infty} \langle W e_k, e_k \rangle = Tr(W) .$$

A similar argument shows that $Tr(A) = Tr(A^1)$. The completeness postulate is crucially used here. Then

$$Tr(AW^1) = \sum_{n=1}^{\infty} Tr\left(A \Lambda_{a_n} W \Lambda_{a_n}\right)$$

$$= \sum_{n=1}^{\infty} Tr\left(\Lambda_{a_n} A W \Lambda_{a_n}\right) \text{ as } A \Lambda_{a_n} = \Lambda_{a_n} A = a_n \Lambda_{a_n}$$

taking $A = \sum a_k \Lambda_{a_k}$

$= Tr(AW)$ by an argument analogus to above.

Then similar arguments give $Tr(AW) = Tr(A^1W) = Tr(A^1W^1)$. This completes the proof of Theorem 5.

Theoram 6

For any response value a_n of an enzyme state A, the probability that A has response value a_n in the state W = the probability that A has response value a_n in the state W^1. Analogous result holds for a substrate state.

Proof :

$$Tr(\Lambda_{a_n} W^1) = \sum_{j} Tr\left(\Lambda_{a_n} \Lambda_{a_j} W \Lambda_{a_j}\right)$$

$$= Tr\left(\Lambda_{a_n} W \Lambda_{a_n}\right)$$

$$= Tr\left(\Lambda_{a_n} W\right) .$$

Similarly,

$$Tr(\Lambda_{w_k} A) = Tr\left(\Lambda_{w_k} A^1\right).$$

Theorem 7

Let A and W be recognition states of an enzyme and a substrate having respective sets of response values (a_n) *and* (w_n) *and having corresponding eigen vectors* (f_n) *and* (e_n) *each forming a complete set. Let* $A \to A^1$ *and* $W \to W^1$ *be a change of states during recognition in induced-fit phenomena. Then each* f_k *is an eigen state of* W^1 *having eigen value*

$$\lambda_k = \sum^{\infty} w_m < e_m, f_k >^2$$

= *average response of W in the state* $f_k \otimes f_k$

= *measure of recognition of* W^1 *by the state* $f_k \otimes f_k$

and each e_k *is an eigen vector of* A^1 *having eigen value*

$$\mu_k = \sum_{m=1}^{\infty} a_m < f_m, e_k >^2$$

= *average response of A in the state* $e_k \otimes e_k$

= *measure of recognition of* A^1 *by the state* $e_k \otimes e_k$.

Proof : Indeed,

$$W = \sum^{\infty} w_n e_n \otimes e_n,$$

$$A = \sum^{\infty} a_m f_m \otimes f_m .$$

Then,

$$W^1 = \sum_n \Lambda_{a_n} W \Lambda_a$$

$$= \sum_{n,m=1}^{\infty} w_m (\Lambda_{a_n} e_m \otimes \Lambda_{a_n} e_m)$$

$$= \sum_{n,m=1}^{\infty} w_m < e_m, f_n >^2 f_n \otimes f_n ,$$

$$A^1 = \sum_{n,m=1}^{\infty} a_m < f_m, e_n >^2 e_n \otimes e_n .$$

Hence, counting the eigen values as per multiplicities,

$$W^1 f_k = \left| \sum^{\infty} w_m < e_m, f_k >^2 \right| f_k ,$$

$$A^1 e_k = \left(\sum_{m=1}^{\infty} a_m < f_m, e_k >^2 \right) e_k .$$

This immediately gives the assertions.

6. Discussion

We have presented a model for the enzyme-substrate recognition in which the recognition state of an enzyme (respectively, a substrate) is represented by a trace class operator A (respectively, W) on an appropriate Hilbert space so that the recognition is achieved by the evaluation of the trace functional $Tr(WA)$. It is also postulated that during recognition, there occurs changes of state $A \to A^1$, $W \to W^1$ incorporating the induced-fit hypothesis in such a way that $A = A^1$ if and only if $W = W^1$ if and only if $AW = WA$ exhibiting the structural complementability so essential for the lock-and-key situation. The present model draws an analogue at a formal level between the process of quantum mechanical measurement and the enzyme-substrate recognition. That the enzyme-substrate recognition can be viewed as a process of measurement was suggested by Edelstein and Rosen [1]. Their model was further explored by Louie *et al* [2]. These models are commutative in nature in the sense that the recognition states are represented by functions. We have shown that the present model does include these previous models; not only that, it refines them by accommodating more complex recognition states represented by operators that are intrinsically non-commutative in nature. These complex states are superposition states of states having well defined response values. The resulting state are complex in the sense that their response values to recognition are only probabilistically defined.

Another advantage of using the non-commutative language of Functional Analysis over the previous models is that the present model incorporates both the dynamical view points of recognition process *viz.* the lock-and-key hypothesis as well as the induced-fit-hypothesis; further, we can describe the situation in which either occurs. The trace functional $Tr(AW)$ provides a quantitative measure of recognition of W by A. The trace property $Tr(AW) =$

$Tr(WA)$ describes the duality between the enzyme and the substrate inherent in the recognition process, whereas the joint continuity of the trace functional $\{A, W\} \rightarrow Tr(AW)$ describes the sensitivity of the recognition. The spectral theory of trace-class operators manifests the indistinguishability characteristic of recognition, the specificity of recognition, existence of complete set of simultaneous recognition states in lock-and-key situation as well as the invariance of recognition under change of state in induced-fit-situation.

References

[1] L Edelstein and R Rosen *J. Theor. Biol.* **73** 181 (1978)

[2] A H Louie, I W Richardson and S Swaminathan *J. Theor. Biol.* **94** 77 (1982)

[3] I W Richardson, A H Louise and S Swaminathan *J. Theor. Biol.* **94** 61 (1982)

[4] M V Volkenstein *Biophysics* (Moscow : Mir) (1983)

[5] A Bohm *Quantum Mechanics* (Berlin : Springer-Verlag) (1980)

[6] S Swaminathan in *Chemical Applications of Topology and Graph Theory* (ed.) R B King (Amsterdam : Elsevier) pp 454-461 (1983)

[7] J Weidmann *Linear Operators in Hilbert Spacer* (New York : Springer-Varlag) (1980)